REMARKS

Claims 1-3, 5-7, and 17-22 are pending in the instant application. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Information Disclosure Statement

The Office Action states that the Information Disclosure Statement submitted December 2, 2003 failed to comply with 37 C.F.R. § 1.97(c) because it lacked the fee set forth in 37 C.F.R. § 1.17(p).

Applicants apologize for this inadvertent omission and hereby authorize the Commissioner to charge the fee set forth in 37 C.F.R. § 1.17(p) to Deposit Account No. 13-2490. Applicants, therefore, seek consideration of the information cited in the Information Disclosure Statement submitted December 2, 2003.

2. Rejections of claims 1-3, 5-7, and 17-22 under 35 U.S.C. § 112, first paragraph

The Office Action maintains a rejection of claims 1-3, 5-7, and 17-22 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the claims do not set forth particular sequences for the probes of the claimed reagent and recite the probes only in terms of their function, the genus of reagents encompassed by the claims includes reagents comprising *any* probe that is specific to any HPV type that is known to cause cancer, and therefore, that the genus of reagents encompassed by the claims includes hundreds of thousands of possible reagents. Specifically, the Action states that the claims encompass reagents comprising any set of *oligonucleotide* probes that is specific to any HPV type that is known to cause cancer. The Action also states that because the specification defines "full length" as permitting some sequence variation and shortening of the probes in the claimed reagents, even claims that recite reagents comprising a set of full length probes are quite broad. The Action also states that because Applicants describe only a single reagent meeting the functional limitations of the claims, Applicants have "express

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possession" of only one species in a genus that comprises hundreds of millions of different possibilities.

In Applicants' response to the Office Action mailed June 26, 2003, claim 1 was amended to recite "a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types but do not detectably hybridize to DNA from non-carcinogenic HPV types" (*emphasis added*). Applicants note that the instant specification describes the HPV probes of the invention as "*essentially full length genomic* HPV probes" having "*essentially* the same sequence as given in GenBank Accession Numbers: K02718 - type 16; X05015 - type 18; J04353 - type 31; M62877 - type 51; M12732 and A12360 - type 33; M74117 - type 35," and that "[w]hile some sequence variations and shortening of the probe length are permitted, *these are still considered full length and are not similar to oligonucleotide probes as used in the prior art*" (page 5, paragraph 1) (*emphasis added*). Applicants also note that the sequences described in GenBank Accession Nos. K02718, X05015, J04353, M62877, M12732, A12360, and M74117 range from 7808 to 7912 nucleotides in length, and that HPV-specific oligonucleotides described in the prior art usually range from 30 to 50 nucleotides in length (*see, e.g.*, International Publication No. WO 95/22626, discussed in section 3 below, which describes HPV-specific oligonucleotides of 23, 25, 28, and 30 nucleotides in length).

Applicants contend that because amended claim 1 recites a reagent comprising a plurality of viral *genomic* HPV DNA probes, the claimed reagent, contrary to the Action's assertion, does not comprise *any* probe that is specific to any HPV type that is known to cause cancer. Applicants also contend that one of ordinary skill in the art, in view of the teachings of the instant application and knowledge in the prior art, would readily understand, for example, that an HPV 16-specific 28-mer oligonucleotide does *not* comprise an *essentially full length* genomic HPV probe having *essentially* the same sequence as that recited in GenBank Accession No. K02718. Applicants further contend that one of ordinary skill in the art would readily understand that a number of reagents comprising a plurality of viral genomic HPV DNA probes could be prepared using the teachings in the instant application and knowledge in the art at the time the instant application was filed.

In view of the teachings in the instant application, Applicants respectfully contend that one of ordinary skill in the art would understand the scope of species comprising the claimed genus of

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reagents, and that the inventors were in possession of the invention having said scope at the time the application was filed. Thus, Applicants respectfully contend that their specification fulfills the requirements of 35 U.S.C. § 112, first paragraph, and request that this ground of rejection be withdrawn.

3. Rejection of claims 1, 2, 5, and 6 under 35 U.S.C. § 102

a. Rejection of claims 1, 2, 5, and 6 as being anticipated by Meijer *et al.*

The Office Action maintains a rejection of claims 1, 2, 5, and 6 under 35 U.S.C. § 102(b), as being anticipated by International Publication No. WO 95/22626 (Meijer *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that because there is no clear indication in the specification regarding the basic and novel characteristics of the invention, the transition phrase "consisting essentially of" in claim 6 has been interpreted as being equivalent to "comprising," and therefore, Meijer *et al.* anticipates claim 6 since Meijer *et al.* disclose that the probe cocktail may be present as two or more different probe mixtures (*i.e.*, smaller groupings of the disclosed probe mixture). The Action also states that the probes disclosed by Meijer *et al.* are full length probes because Meijer *et al.* disclose the entire sequence of each probe and that the full length of the probe is to be used in preparing the reagent.

As discussed in section 2 above, the instant specification teaches that the HPV probes of the invention are "*essentially full length genomic* HPV probes" that "are *not* similar to oligonucleotide probes as used in the prior art" (page 5, paragraph 1) (*emphasis added*). As also described in section 2 above, in Applicants' response to the Office Action mailed June 26, 2003, claim 1 was amended to recite "a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types but do not detectably hybridize to DNA from non-carcinogenic HPV types" (*emphasis added*). Applicants note that Meijer *et al.*, on the other hand, disclose *oligonucleotide* primers of only 23-28 nucleotides for amplifying HPV DNA present in a sample by polymerase chain reaction, and *oligonucleotide* probes of only 30 nucleotides for HPV genotyping of

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the amplification product. Applicants contend, therefore, that while the reagent of Meijer *et al.* comprises *only* HPV-specific *oligonucleotide* probes, the reagent of amended claim 1 comprises viral *genomic* HPV DNA probes (*i.e.*, HPV-specific *polynucleotide* probes). Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, Meijer *et al.* cannot anticipate claims 1, 2, 5, and 6.

In addition, Applicants respectfully disagree with the Action's assertion that since Meijer *et al.* disclose the entire sequence of their probes and that the entire length of their probes are to be used, the probes disclosed by Meijer *et al.* are *full length* probes. Applicants contend that because Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides – or *only* about 0.38% of the HPV genome (*i.e.*, the HPV genome comprising nearly 8000 nucleotides) – Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that the Action's interpretation of the term "full length probes" contradicts both the *explicit* disclosure of the instant application – which teaches that the HPV probes of the invention are "*essentially full length genomic* HPV probes" that "are *not* similar to oligonucleotide probes as used in the prior art" – and the understanding of those of ordinary skill in the art. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, Meijer *et al.* cannot anticipate claims 1, 2, 5, and 6. Withdrawal of this rejection is therefore respectfully solicited.

b. Rejection of claims 1 and 5 as being anticipated by Troncone *et al.*

The Office Action also maintains a rejection of claims 1 and 5 under 35 U.S.C. § 102(b), as being anticipated by Troncone *et al.*, 1992, *J. Clin. Pathol.* 45:308-313. The Action states that Troncone *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Troncone *et al.* disclose a reagent comprising full length genomic probes that are specific for HPV types 16, 18, and 33.

Applicants note that Troncone *et al.* disclose a non-isotopic *in situ* hybridization (NISH) study in which samples were first analyzed in *separate* hybridizations with "genomic HPV probes" corresponding to HPV types 6/11, 16, 18, and 33 (page 309), and then because no samples tested positive for HPV types 6 or 11 (page 312, Table 3), the samples were re-examined by hybridization

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with "[a] cocktail of HPV 16, 18, and 33 probes" (page 309). Applicants contend that because *none* of the samples analyzed by Troncone *et al.* tested positive for HPV types 6 or 11 (*i.e.*, non-carcinogenic types), this reference does not disclose "a plurality of viral genomic HPV DNA probes that . . . do not detectably hybridize to DNA from non-carcinogenic HPV types." Moreover, because the exact nature of the probe cocktail used by Troncone *et al.* cannot be clearly inferred from the reference (indeed, as discussed below, it cannot be clearly inferred from the reference whether the probes used by Troncone *et al.* are even full length probes), one of ordinary skill in the art cannot predict whether the probe cocktail used by Troncone *et al.* would cross react with non-carcinogenic HPV types. Applicants contend, therefore, that because Troncone *et al.* does not disclose a probe cocktail known to specifically hybridize to only carcinogenic HPV types, a probe cocktail that detectably hybridizes to DNA from a plurality of carcinogenic HPV types but does not detectably hybridize to DNA from non-carcinogenic HPV types does not "necessarily flow[] from the teachings of the applied prior art," as it is required to do to properly anticipate the pending claims. *Ex parte Levy*, 17 U.S.P.Q.2d (BNA) 1461, 1464 (B.P.A.I. 1990). Moreover, Applicants contend that while it is clear that Troncone *et al.*, in their initial analysis, used four genomic HPV probes (including a genomic probe that recognizes the non-carcinogenic HPV types 6/11), it cannot be clearly inferred from the reference that the probes in the HPV 16/18/33 cocktail were *genomic* probes, as opposed to *oligonucleotide* probes. Applicants contend that because Troncone *et al.* does not disclose "a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types *but do not detectably hybridize to DNA from non-carcinogenic HPV types*" (*emphasis added*), Troncone *et al.* does not anticipate claims 1 and 5. Withdrawal of this rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

4. Rejections of claims 1-3, 5-7, and 17-22 under 35 U.S.C. § 103

a. Rejection of claim 3 as being unpatentable over Meijer *et al.* in view of Orth *et al.*

The Office Action maintains a rejection of claim 3 under 35 U.S.C. § 103(a), as being

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unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,981,173 (Orth *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be supplemented with additional probes as new high-risk HPV types are identified. The Action further states that Meijer *et al.* do not disclose a reagent that hybridizes to HPV types 68 and 70, but that Orth *et al.* disclose the genomes of HPV types 68 and 70 and oligonucleotide probes for the detection of HPV types 68 and 70. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the probes disclosed by Orth *et al.* in the reagent disclosed by Meijer *et al.*

As discussed in section 3 above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. In addition, Orth *et al.* disclose oligonucleotide probes for the detection of HPV types 68 and 70, rather than essentially full length genomic probes. Applicants contend that because neither Meijer *et al.* nor Orth *et al.* disclose the use of essentially full length genomic probes, the genus of reagents defined by the pending claims does not encompass the oligonucleotide probe reagent disclosed by Meijer *et al.* in view of Orth *et al.*, and therefore, Meijer *et al.* in view of Orth *et al.* does not result in a *prima facie* case of obviousness with respect to claim 3. Withdrawal of this rejection is therefore respectfully solicited.

b. Rejection of claim 7 as being unpatentable over Meijer *et al.* in view of Bauer *et al.*

The Office Action also maintains a rejection of claim 7 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,639,871 (Bauer *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that

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Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose reagents comprising smaller groupings of HPV probes. The Action further states that Meijer *et al.* do not disclose a reagent comprising probes that are present in the proportions recited in claim 7, but that the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made (as exemplified by Bauer *et al.*). The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different probe concentrations so as to arrive at an optimal concentration for the detection of HPV in a sample.

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, claim 7 does not encompass optimized hybridization assays that use the reagent disclosed by Meijer *et al.*, and therefore, Meijer *et al.* in view of Bauer *et al.* does not result in a *prima facie* case of obviousness with respect to claim 7. Withdrawal of this rejection is therefore respectfully solicited.

c. Rejection of claims 17, 18, 20, and 21 as being unpatentable over Meijer *et al.* in view of the 1988 Stratgene Catalog

The Office Action also maintains a rejection of claims 17, 18, 20, and 21 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of the 1988 Stratagene Catalog. The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose reagents comprising smaller groupings of HPV probes. The Action further states that the probes disclosed by Meijer *et al.* are full length probes because Meijer *et al.* disclose the entire sequence of each probe and that the full length of the probe is to be used in preparing the reagent. The Action also states that Meijer *et al.* do not

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disclose kits wherein reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagent disclosed by Meijer *et al.* into containers for distribution in a kit.

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, claims 17, 18, 20, and 21 do not encompass a kit containing the reagent disclosed by Meijer *et al.*, and therefore, Meijer *et al.* in view of the 1988 Stratagene Catalog does not result in a *prima facie* case of obviousness with respect to claims 17, 18, 20, and 21. Withdrawal of this rejection is therefore respectfully solicited.

d. Rejection of claims 17 and 20 as being unpatentable over Troncone *et al.* in view of the 1988 Stratgene Catalog

The Office Action also maintains a rejection of claims 17 and 20 under 35 U.S.C. § 103(a), as being unpatentable over Troncone *et al.*, 1992, *J. Clin. Pathol.* 45:308-313, in view of the 1988 Stratagene Catalog. The Action states that Troncone *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Troncone *et al.* disclose a reagent comprising full length genomic probes that are specific for HPV types 16, 18, and 33. The Action also states that Troncone *et al.* do not disclose kits wherein reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagent disclosed by Troncone *et al.* into containers for distribution in a kit.

As discussed in section 3 above, Troncone *et al.* disclose a non-isotopic *in situ* hybridization (NISH) study in which samples were first analyzed in *separate* hybridizations with "genomic HPV probes" corresponding to HPV types 6/11, 16, 18, and 33 (page 309), and then because no samples tested positive for HPV types 6 or 11 (page 312, Table 3), the samples were re-examined by

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hybridization with "[a] cocktail of HPV 16, 18, and 33 probes" (page 309). Applicants contend that because *none* of the samples analyzed by Troncone *et al.* tested positive for HPV types 6 or 11 (*i.e.*, non-carcinogenic types), this reference does not disclose "a plurality of viral genomic HPV DNA probes that . . . do not detectably hybridize to DNA from non-carcinogenic HPV types." Moreover, because the exact nature of the probe cocktail used by Troncone *et al.* cannot be clearly inferred from the reference (indeed, as discussed below, it cannot be clearly inferred from the reference whether the probes used by Troncone *et al.* are even full length probes), one of ordinary skill in the art cannot predict whether the probe cocktail used by Troncone *et al.* would cross react with non-carcinogenic HPV types. Applicants contend, therefore, that because Troncone *et al.* does not disclose a probe cocktail known to specifically hybridize to only carcinogenic HPV types, a probe cocktail that detectably hybridizes to DNA from a plurality of carcinogenic HPV types but does not detectably hybridize to DNA from non-carcinogenic HPV types does not "necessarily flow[] from the teachings of the applied prior art." *Ex parte Levy*, 17 U.S.P.Q.2d (BNA) 1461, 1464 (B.P.A.I. 1990). Moreover, Applicants contend that while it is clear that Troncone *et al.*, in their initial analysis, used four genomic HPV probes (including a genomic probe that recognizes the non-carcinogenic HPV types 6/11), it cannot be clearly inferred from the reference that the probes in the HPV 16/18/33 cocktail were *genomic* probes, as opposed to *oligonucleotide* probes. Applicants contend that because Troncone *et al.* does not disclose a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types *but do not detectably hybridize to DNA from non-carcinogenic HPV types*, claims 17 and 20 do not encompass a kit containing the reagent disclosed by Troncone *et al.*, and therefore, Troncone *et al.* in view of the 1988 Stratagene Catalog does not result in a *prima facie* case of obviousness with respect to claims 17 and 20. Withdrawal of this rejection is therefore respectfully solicited.

e. Rejection of claim 19 as being unpatentable over Meijer *et al.* in view of Orth *et al.* and the 1988 Stratgene Catalog

The Office Action also maintains a rejection of claim 19 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,981,173 (Orth *et al.*), and further in view of the 1988 Stratagene Catalog. The Action states

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that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be supplemented with additional probes as new high-risk HPV types are identified. The Action further states that Meijer *et al.* do not disclose a reagent that hybridizes to HPV types 68 and 70, but that Orth *et al.* disclose the genomes of HPV types 68 and 70 and oligonucleotide probes for the detection of HPV types 68 and 70. The Action also states that Meijer *et al.* in view of Orth *et al.* does not disclose kits wherein reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagent disclosed by Meijer *et al.* in view of Orth *et al.* into containers for distribution in a kit.

As discussed above, neither Meijer *et al.* nor Orth *et al.* disclose the use of essentially full length genomic probes, and therefore, the combination does not result in a *prima facie* case of obviousness. Applicants contend that because Meijer *et al.* in view of Orth *et al.* does not disclose the use of essentially full length genomic probes, claim 19 does not encompass a kit containing the reagent disclosed by Meijer *et al.* in view of Orth *et al.*, and therefore, Meijer *et al.* in view of Orth *et al.*, and further in view of the 1988 Stratagene Catalog, does not result in a *prima facie* case of obviousness with respect to claim 19. Withdrawal of this rejection is therefore respectfully solicited.

f. Rejection of claim 22 as being unpatentable over Meijer *et al.* in view of Bauer *et al.* and the 1988 Stratgene Catalog

The Office Action also maintains a rejection of claim 22 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,639,871 (Bauer *et al.*), and further in view of the 1988 Stratagene Catalog. The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific

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for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose reagents comprising smaller groupings of HPV probes. The Action further states that Meijer *et al.* do not disclose a reagent comprising probes that are present in the proportions recited in claim 7, but that the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made (as exemplified by Bauer *et al.*). The Action also states that Meijer *et al.* in view of Bauer *et al.* does not disclose kits wherein reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagent disclosed by Meijer *et al.* in view of Bauer *et al.* into containers for distribution in a kit.

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, claim 22 does not encompass a kit containing the reagent disclosed by Meijer *et al.* for use in optimized hybridization assays, and therefore, Meijer *et al.* in view of Bauer *et al.*, and further in view of the 1988 Stratagene Catalog does not result in a *prima facie* case of obviousness with respect to claim 22. Withdrawal of this rejection is therefore respectfully solicited.

g. Rejection of claims 1, 2, 5, and 6 as being unpatentable over Meijer *et al.* in view of Faulkner-Jones *et al.*

The Office Action asserts a rejection of claims 1, 2, 5, and 6 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of Faulkner-Jones *et al.*, 1993, *J. Virol. Methods* 41:277-96. The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be

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supplemented with additional probes as new high-risk HPV types are identified. The Action also states that Meijer *et al.* disclose reagents comprising smaller groupings of HPV probes. The Action further states that the probes disclosed by Meijer *et al.* are full length probes because Meijer *et al.* disclose the entire sequence of each probe and that the full length of the probe is to be used in preparing the reagent. The Action also states that Meijer *et al.* do not disclose a reagent in which the probes are "viral genomic HPV DNA probes" and the genomic HPV DNA probes are entire HPV genomes, but that Faulkner-Jones *et al.* disclose reagents for detecting HPV in samples and methods for isolating whole genomic probes, and further, disclose that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes because full length genomic probes are more sensitive than oligonucleotide probes. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the reagent disclosed by Meijer *et al.* so as to have provided a reagent comprising whole genomic probes as disclosed by Faulkner-Jones *et al.*

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Moreover, Applicants respectfully disagree with the Action's assertion that Faulkner-Jones *et al.* disclose that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes because full length genomic probes are more sensitive than oligonucleotide probes. Instead, Faulkner-Jones *et al.* disclose that (a) oligonucleotide probes provide a useful alternative to full length probes for clinical detection and typing of HPV due to the ease, speed, and relatively low cost of preparing, labeling, and using oligonucleotide probes; (b) oligonucleotide probes were found to be more sensitive than full length probes in Northern hybridizations; and (c) the sensitivity of oligonucleotide probes could be increased by simply using two oligonucleotide probes for each viral type, and further, that when two oligonucleotide probes were used, the oligonucleotide probes were found to be three to five times more sensitive than full length probes in dot blots (page 293). Applicants contend, therefore, that the Faulkner-Jones *et al.* reference actually teaches away from the use of full length genomic probes. Because Meijer *et al.* does not disclose the use of essentially full length genomic probes, and further, because Faulkner-Jones *et al.* do not disclose that HPV DNA detection using full length genomic

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probes is preferred over oligonucleotide probes, Applicants contend that the genus of reagents defined by claims 1, 2, 5, and 6 does not encompass the reagent disclosed by Meijer *et al.* in view of Faulkner-Jones *et al.*, and therefore, Meijer *et al.* in view of Faulkner-Jones *et al.* does not result in a *prima facie* case of obviousness with respect to claims 1, 2, 5, and 6. Withdrawal of this rejection is therefore respectfully solicited.

h. Rejection of claims 1, 2, 5, and 6 as being unpatentable over Meijer *et al.* in view of Faulkner-Jones *et al.* and Orth *et al.*

The Office Action also asserts a rejection of claims 1, 2, 5, and 6 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of Faulkner-Jones *et al.*, 1993, *J. Virol. Methods* 41:277-96, and further in view of U.S. Patent No. 5,981,173 (Orth *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be supplemented with additional probes as new high-risk HPV types are identified. The Action also states that Meijer *et al.* disclose reagents comprising smaller groupings of HPV probes. The Action further states that Meijer *et al.* do not disclose a reagent that hybridizes to HPV types 68 and 70, but that Orth *et al.* disclose the genomes of HPV types 68 and 70 and oligonucleotide probes for the detection of HPV types 68 and 70. The Action also states that Meijer *et al.* do not disclose a reagent in which the probes are "viral genomic HPV DNA probes" and the genomic HPV DNA probes are entire HPV genomes, but that Faulkner-Jones *et al.* disclose reagents for detecting HPV in samples and methods for isolating whole genomic probes, and further, that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes because full length genomic probes are more sensitive than oligonucleotide probes. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the probes disclosed by Orth *et al.* in the reagent disclosed by Meijer *et al.* in view of Faulkner-Jones *et al.*

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As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. In addition, Orth *et al.* disclose oligonucleotide probes for the detection of HPV types 68 and 70, rather than essentially full length genomic probes. Moreover, Applicants respectfully disagree with the Action's assertion that Faulkner-Jones *et al.* disclose that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes because full length genomic probes are more sensitive than oligonucleotide probes. Instead, Faulkner-Jones *et al.* disclose that (a) oligonucleotide probes provide a useful alternative to full length probes for clinical detection and typing of HPV due to the ease, speed, and relatively low cost of preparing, labeling, and using oligonucleotide probes; (b) oligonucleotide probes were found to be more sensitive than full length probes in Northern hybridizations; and (c) the sensitivity of oligonucleotide probes could be increased by simply using two oligonucleotide probes for each viral type, and further, that when two oligonucleotide probes were used, the oligonucleotide probes were found to be three to five times more sensitive than full length probes in dot blots (page 293). Applicants contend, therefore, that the Faulkner-Jones *et al.* reference actually teaches away from the use of full length genomic probes. Because neither Meijer *et al.* nor Orth *et al.* disclose the use of essentially full length genomic probes, and further, because Faulkner-Jones *et al.* do not disclose that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes, Applicants contend that the genus of reagents defined by claims 1, 2, 5, and 6 does not encompass the oligonucleotide probe reagent disclosed by Meijer *et al.* in view of Faulkner-Jones *et al.*, and further in view of Orth *et al.*, and therefore, Meijer *et al.* in view of Faulkner-Jones *et al.*, and further in view of Orth *et al.*, does not result in a *prima facie* case of obviousness with respect to claims 1, 2, 5, and 6. Withdrawal of this rejection is therefore respectfully solicited.

i. Rejection of claim 7 as being unpatentable over Meijer *et al.* in view of Faulkner-Jones *et al.* and Bauer *et al.*

The Office Action also asserts a rejection of claim 7 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of Faulkner-Jones *et al.*, 1993, *J. Virol. Methods* 41:277-96, and further in view of U.S. Patent No. 5,639,871

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(Bauer *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* do not disclose a reagent in which the probes are "viral genomic HPV DNA probes" and the genomic HPV DNA probes are entire HPV genomes, but that Faulkner-Jones *et al.* disclose reagents for detecting HPV in samples and methods for isolating whole genomic probes, and further, that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes because full length genomic probes are more sensitive than oligonucleotide probes. The Action further states that Meijer *et al.* do not disclose a reagent comprising probes that are present in the proportions recited in claim 7, but that the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made (as exemplified by Bauer *et al.*). The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different concentrations of the reagent disclosed by Meijer *et al.* in view of Faulkner-Jones *et al.* so as to arrive at an optimal concentration for the detection of HPV in a sample.

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Moreover, Applicants respectfully disagree with the Action's assertion that Faulkner-Jones *et al.* disclose that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes because full length genomic probes are more sensitive than oligonucleotide probes. Instead, Faulkner-Jones *et al.* disclose that (a) oligonucleotide probes provide a useful alternative to full length probes for clinical detection and typing of HPV due to the ease, speed, and relatively low cost of preparing, labeling, and using oligonucleotide probes; (b) oligonucleotide probes were found to be more sensitive than full length probes in Northern hybridizations; and (c) the sensitivity of oligonucleotide probes could be increased by simply using two oligonucleotide probes for each viral type, and further, that when two oligonucleotide probes were used, the oligonucleotide probes were found to be three to five times more sensitive than full length probes in dot blots (page 293). Applicants contend, therefore, that the

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Faulkner-Jones *et al.* reference actually teaches away from the use of full length genomic probes. Because Meijer *et al.* does not disclose the use of essentially full length genomic probes, and further, because Faulkner-Jones *et al.* do not disclose that HPV DNA detection using full length genomic probes is preferred over oligonucleotide probes, Applicants contend that claim 7 does not encompass optimized hybridization assays that use the reagent disclosed by Meijer *et al.* in view of Faulkner-Jones *et al.*, and therefore, Meijer *et al.* in view of Faulkner-Jones *et al.*, and further in view of Bauer *et al.*, does not result in a *prima facie* case of obviousness with respect to claim 7. Withdrawal of this rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 103 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Switzer believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
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By: 
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